Journal of Obsessive-Compulsive and Related Disorders 2 (2013) 221–231

Contents lists available at SciVerse ScienceDirect

Journal of Obsessive-Compulsive and Related Disorders

journal homepage: www.elsevier.com/locate/jocrd

Lifetime comorbidity of obsessive-compulsive disorder and sub-threshold obsessive-compulsive symptomatology in the community: impact, prevalence, socio-demographic and clinical characteristics

N.A. Fineberg, M.P. Hengartner, C. Bergbaum, T.M. Gale, K. Jefferies, W. Rössler, J. Angst

Background

The nosological status of obsessive-compulsive disorder (OCD) is currently under review. In the National Comorbidity Survey replication (NCS-R) of US adults, OCD was strongly associated with anxiety, mood, impulse-control and substance use disorders. Data from the Epidemiological Catchment Area (ECA) Study and the NSC-R also identified a greater likelihood of bipolar (especially bipolar-II) disorder comorbidity, compared with major depressive disorder in OCD. This study expands the available knowledge on OCD-comorbidity by investigating the prevalence and clinical impact on a group of individuals with OCD or subthreshold OC syndrome (OCS), prospectively followed-up over an extended period.

Methods: A stratified sample of the general population of Zurich, consisting of 591 subjects (292 males; 299 females) participated in a series of seven interviews over a 30-year period from age 20–50years. Psychologists or psychiatrists interviewed participants in their homes using the SPIKE, a face-to-face interview based upon DSM-criteria that covered the previous twelve months. The number and percentage of comorbid disorders were analysed with contingency tables. Odds ratios and their 95% confidence intervals were estimated with series of bivariate binary logistic regression models. Longitudinal associations between repeated distress and lifetime comorbid disorders were examined with generalized estimating equations. Individuals with OC states, with and without comorbidity, were compared to determine differences in socio-demographic factors, clinical characteristics, levels of distress, functional impairment, suicidality and treatment. Factors related to comorbidity were examined with series of multivariate logistic regression models. Meaningful and multivariately predominant predictors were extracted through the backward stepwise (Wald) exclusion method.

Results: Over the study period, 30 subjects, 11 males and 19 females (63%), were diagnosed with OCD, 98 with OCS and 107 with OC symptoms. Lifetime rates of psychiatric comorbidity were high and increased in prevalence across the OC severity spectrum.

As many as 73% of individuals with OCD experienced an anxiety disorder and 60% an affective disorder. When compared to controls (i.e. subjects without any OC symptoms), the lifetime rates of several disorders were significantly associated with OCD(specifically, generalised anxiety disorder (GAD) 50%, $p < 0.01$; social phobia 40%, $p < 0.01$; agoraphobia 30%, $p < 0.01$; panic disorder 17%, $p < 0.05$; bipolar disorder 40%, $p < 0.01$), whereas unipolar major depression and both alcohol and drug misuse disorders were not significantly more frequently associated with any diagnosis of OC severity-spectrum disorders. Most forms of comorbidity increased distress and impacted negatively on family and work relationships, though disorder-specific effects were observed. Thus, bipolar disorder, agoraphobia and GAD were associated with increased OCD-severity; bipolar disorder was associated with increased substance abuse and suicidal acts and panic disorder with increased treatment-seeking behaviour.

Discussion: In a population-based sample, lifetime rates of psychiatric comorbidity were high and increased in prevalence across the OC severity spectrum. The American Psychiatric Association is actively considering removing OCD from the Anxiety Disorders group, where it is categorised in the DSM-IV (www.dsm5.org/). Comorbidity, per se, does not necessarily imply shared aetiology. The magnitude of the association that was found in this study between a broad range of anxiety disorders and OCD, which exceeded the association with lesser OC states, hints that one distinction between OCD and sub-threshold OC symptoms might involve the recruitment of neuropsychological mechanisms linked to pathological anxiety in the full-blown disorder, either as a causal or consequential factor. From a neuropsychological perspective, our finding of a specific relationship between OC states and bipolarity is intriguing and is consistent with the existence of as yet poorly defined, overlapping response-inhibition deficits that could possibly play an aetiological role both in the development of these disorders and in the progression to substance abuse and suicidal acts. These hypotheses merit further exploration using translational paradigms.

2211-3649/$ - see front matter
http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Social Phobia in Obsessive-Compulsive Disorder: Prevalence and Correlates

Assunção M.C.[a], Costa D.C.[b], Mathis M.A.[b], Shavitt R.G.[b], Ferrão Y. A.[c], Rosário M.C.[d], Miguel E.C.[b], Torres A.R.[a]

[a] *Departament of Neurology, Psychology and Psychiatry, Botucatu Medical School, São Paulo State University (UNESP)*
[b] *Department and Institute of Psychiatry, São Paulo University Medical School*
[c] *Federal University of Health Sciences, Porto Alegre (RS)*
[d] *Department of Psychiatry, Federal University of São Paulo.*

Background

Social Phobia (SP) is an anxiety disorder that frequently co-occurs with obsessive-compulsive disorder (OCD); however, studies that evaluate clinical factors associated with this specific comorbidity are rare. The aim was to estimate the prevalence of SP in a large multicenter sample of OCD patients and compare the characteristics of individuals with and without SP.

Method: A cross-sectional study with 1001 patients of the Brazilian Research Consortium on Obsessive-Compulsive Spectrum Disorders using several assessment instruments, including the Dimensional Yale-Brown Obsessive-Compulsive Scale and the Structured Clinical Interview for DSM-IV Axis I Disorders. Univariate analyses were followed by logistic regression.

Results: Lifetime prevalence of SP was 34.6% (N = 346). The following variables remained associated with SP comorbidity after logistic regression: male sex, lower socioeconomic status, body dysmorphic disorder, specific phobia, dysthymia, generalized anxiety disorder, agoraphobia, Tourette syndrome and binge eating disorder.

Limitations: The cross-sectional design does not permit the inference of causal relationships; some retrospective information may have been subject to recall bias; all patients were being treated in tertiary services, therefore generalization of the results to other samples of OCD sufferers should be cautious. Despite the large sample size, some hypotheses may not have been confirmed due to the small number of cases with these characteristics (type 2 error).

Conclusion: SP is frequent among OCD patients and co-occurs with other disorders that have common phenomenological features. These findings have important implications for clinical practice, indicating the need for broader treatment approaches for individuals with this profile.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Comorbid depression in treatment-refractory OCD. Prevalence, severity and outcome data for 179 patients

Himanshu Tyagi, MRCPsych, Rupal Patel, MRCPsych

Lynne Drummond MRCP MRCPsych OCD & BDD Service, Springfield University Hospital, 61 Glenburnie Road, London SW17 7DJ United Kingdom

Background

Depression is the most common clinical comorbidity in Obsessive Compulsive Disorder (OCD). Evidence suggests that up to two-thirds of all patients with OCD can suffer from comorbid depression. In addition it is widely believed that comorbid depression with OCD leads to a poorer outcome for treatment. This belief might have some scientific credence as depression is shown to impair habituation response, which is required for a successful exposure and response prevention (EXRP). However, this question has been poorly researched in the specific context of treatment refractory OCD. This study investigated the prevalence of comorbid depression in patients diagnosed with treatment refractory OCD. As a secondary objective it compared the response to standard treatment between the depressed and non-depressed OCD patients.

Method: Our sample constituted of all patients with a primary diagnosis of treatment refractory OCD who were accepted for outpatient treatment at a specialist OCD service in London between 1st January 2008 and 30th June 2010. Standardised clinician rated and self-report measures for assessment of the severity of OCD and depression were completed at regular intervals (assessment, mid-treatment, discharge from active treatment, 1 month post discharge, 3 months post-discharge, 6 month post discharge, 12 months post discharge). Yale Brown Obsessive Compulsive Scale (YBOCS Version 1.0) was used as the primary measure to assess the severity of OCD. The symptoms and severity of co-morbid depression were assessed by using Beck Depression Inventory (BDI) and Montgomery Asberg Depression Rating Scale (MADRS). As a secondary measure, PADUA inventory was used to assess the nature of the symptoms of OCD. In addition, routinely collected social and demographic data was also used to explore the role of any additional factors.

Results: 165 (92.2%) patients out of a total sample of 179 patients with treatment-refractory OCD were found to have clinically significant depression. This is significantly higher than the prevalence reports of 60–70% of comorbid depression in all patients of OCD. To our knowledge, this is the first such estimate of the prevalence of depression in a population with treatment refractory OCD. Presence of comorbid depression did not influence the treatment response. Improvement in depression is significantly correlated with a successful treatment response ($p < 0.001$). The average improvement in BDI score was 39.5% (SD 43.0%). The average improvement in YBOCS score was 36.5% (SD 36.9%).

The average improvement in the following factors were not found to be significantly associated with

successful treatment response: age of onset of OCD, duration of OCD, comorbid depression at assessment, severity of depression at assessment, number of CBT sessions, gender.

References: 1. Timpano KR, Rubenstein LM, Murphy DL. Phenomenological features and clinical impact of affective disorders in OCD: a focus on the bipolar disorder and OCD connection. Depress Anxiety 2011 Nov 22. doi: 10.1002/da.20908.

2. Quarantini LC, Torres AR, Sampaio AS, Fossaluza V, Mathis MA et al. Comorbid major depression in obsessive-compulsive disorder patients. Compr Psychiatry 2011 Jul-Aug;52(4):386–93.

3. Abramowitz JS. Treatment of obsessive-compulsive disorder in patients who have comorbid major depression. J Clin Psychol 2004 Nov;60(11):1133-41.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Substance use in obsessive-compulsive disorder: what does it mean?

Natalie L. Cuzen [a,b,c], Christine Lochner [d], Joseph Zohar [e], Dan J. Stein [a,d], Naomi A. Fineberg [c,f]

[a] *University of Cape Town, Department of Psychiatry and Mental Health, Observatory, 7925, South Africa*
[b] *University of Cape Town, Department of Psychology, ACSENT Laboratory, Rondebosch, 7701, South Africa*
[c] *University of Hertfordshire, Postgraduate Medical School, College Lane, Hatfield, Hertfordshire, AL10 9AB*
[d] *MRC Unit on Anxiety and Stress Disorders, University of Stellenbosch, Department of Psychiatry, Tygerberg, 7505, South Africa*
[e] *Chaim Sheba Medical Centre, Department of Psychiatry, Tel-Hashomer, 52621, Israel*
[f] *National Obsessive Compulsive Disorders Specialist Service, Hertfordshire Partnership NHS Foundation Trust, Queen Elizabeth II Hospital, Welwyn Garden City, AL7 4HQ*

Background

Individuals with obsessive-compulsive disorder (OCD) may be generally less inclined than those unaffected with the disorder to engage in risky or impulsive behaviours, such as substance use. Cohort studies have generally shown no elevation of substance use disorder (SUD) rates in treatment-seeking OCD patients. Interestingly, some but not all epidemiological studies have shown elevated rates of SUDs among OCD patients compared with controls. We aimed to investigate the prevalence and possible impact of SUDs within a large cohort of individuals with OCD.

Methods: Survey data were derived from the ICOCS database, a large-scale, multi-centre (10 centres across Europe, Canada, Africa, the Americas, and the Middle East) database of treatment-seeking individuals with current OCD ($n = 445$). Measures relevant to the current investigation include the Mini International Neuropsychiatric Inventory, the Yale-Brown Obsessive Compulsive Scale, as well as a demographics questionnaire.

Results: Rates for alcohol abuse ($n = 12$; 2.7%), alcohol dependence ($n = 7$; 1.6%), as well as other drug abuse ($n = 1$; 0.2%) and dependence ($n = 2$; 0.4%) were low. Graphical inspection of the data did not reveal any obvious differences in SUD prevalence by geographical location. Owing to such low numbers, the ability to detect possible significance in SUD-related group differences was limited. Nevertheless, those with OCD and comorbid SUD had numerically more severe OCD symptoms (YBOCS total score: $M = 24.53$, $SD = 4.21$) compared to those without comorbid SUD ($M = 22.44$, $SD = 7.23$; n.s.). In addition, the former group also reported higher incidence of past depressive episodes (56%) than the latter group (39%). Incidence of past depressive episodes was not associated with differences in OCD severity, and no other associations could be observed.
Discussion: These data indicate that SUDs are infrequent among individuals with OCD, representing a rate reduced by approximately 50% of that for the normal population. Avoidance of substance use in OCD appears to be unaffected by cultural and geographical divides. SUD comorbidity may possibly be associated with greater OCD severity, as well as a history of more depressive episodes. In summary, reduced SUD rate in this cohort supports long-standing observations of elevated and generalized harm avoidance tendencies among individuals with OCD, which requires further exploration in OCD with and without SUD comorbidity.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Prevalence of Smoking in Obsessive Compulsive Disorder (OCD)

Himanshu Tyagi, MRCPsych, Sheetal Sirohi, MRCPsych, Lynne M Drummond, MRCP MRCPsych

OCD & BDD Service, Springfield University Hospital, 61 Glenburnie Road, London SW17 7DJ United Kingdom

Background

People with an existing mental illness have a higher prevalence of smoking tobacco products. In England, 32% of people with a common mental disorder smoke regularly as compared with 20% of people without a mental illness (1). More than half (57%) of people attempting suicide in the past year are also reported to be smokers (1). Current research suggests that smoking rates may vary with type of mental illnesses. The highest incidence of smoking has been reported in psychotic illness, followed by affective disorders. There is a scarcity of research into the prevalence of smoking in Obsessive Compulsive Disorder (OCD). In addition there are contradictory reports on the rates of smoking in OCD, with some researchers reporting it as significantly less than that of the general population and others more in line with the rates seen in other anxiety disorders and depression. In addition, the differences in the prevalence of smoking have not been examined in the context of the severity of the illness.
Method: The sample for this study constituted of all patients with a primary diagnosis of OCD, who obtained outpatient treatment from a specialist OCD service in southwest London between April 2009 and April 2010 (n=154). The rate of smoking in this sample was compared with another large sample consisting of people receiving outpatient treatment for serious mental illness (psychosis or treatment refractory depression) from a community mental health team (CMHT) based in the same geographical area (n=324). Smoking data for every patient in our sample was captured via the clinicians responsible for the care of that individual. The severity of OCD was determined by using Yale-Brown Obsessive Compulsive Scale (Version 1), which is a standardised measure.
Results: Patient with severe to profound OCD (YBOCS > 30) were less likely to be a current smoker than patients with moderate OCD (YBOCS 16–30), other psychiatric illnesses or the general population in England ($p < 0.05$). However there is no significant difference between the smoking rates between the general population and moderate to severe OCD. No statistically significant difference was found between the severity of OCD or depression symptoms in current smokers and non-smokers.
Reference: 1. Adult

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Clinical Features of "Pure" Obsessive-Compulsive Disorder

Torres A.R., Shavitt R.G., Torresan R.C., Ferrão Y.A., Miguel E.C., Fontenelle L.F.

Background

Psychiatric comorbidity is the rule in obsessive-compulsive disorder (OCD). However, very few studies have evaluated the clinical characteristics of patients with no co-occurring disorders (non-comorbid or "pure" OCD). The aim of this study was to estimate the prevalence of "pure" cases in a large multicenter sample of OCD patients and to compare socio-demographic and clinical characteristics of individuals with and without any lifetime axis I comorbidity.
Method: Cross-sectional study with 955 adult patients of the Brazilian Research Consortium on Obsessive-Compulsive Spectrum Disorders (C-TOC). Assessment instruments included the Yale-Brown Obsessive-Compulsive Scale, the Dimensional Yale-Brown Obsessive-Compulsive Scale, The USP-Sensory Phenomena Scale and the Brown Assessment of Beliefs Scale. Comorbidities were evaluated using the Structured Clinical Interview for DSM-IV Axis I Disorders. Bivariate analyses were followed by logistic regression.
Results: Only 74 patients (7.7%) presented "pure" OCD. Compared to those presenting at least one lifetime comorbidity (881, 92.3%), non-comorbid patients were more likely to be female and to be working, reported less traumatic experiences and presented lower scores in the Y-BOCS obsession subscale and in total DY-BOCS scores. All symptom dimensions, except contamination-cleaning and hoarding, were less severe in non-comorbid patients. They also presented less severe depression and anxiety, lower suicidality and less previous treatments. In the logistic regression, the following variables predicted pure OCD: sex, severity of depressive and anxious symptoms, previous suicidal thoughts and no previous psychotherapy.
Conclusions: "Pure" OCD patients were the minority in this large sample and were characterized by female sex, less severe depressive and anxious symptoms, less suicidal thoughts, and fewer use of psychotherapy as a modality of treatment. Implications of these findings for clinical practice are discussed.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Thirty years of clinical trials in obsessive compulsive disorder: Excluding the 'true' patient?

Odlaug B.L.[a,b], Weinhandl E.[c], Mancebo M.C.[d], Eisen J.L.[d], Rasmussen S.A.[d], Schreiber L.R.N.[e], Grant J.E.[b]

[a] *Department of Public Health, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark*

[b] *Department of Psychiatry and Behavioral Neuroscience, University of Chicago, Chicago, IL, USA*
[c] *Chronic Disease Research Group, Minneapolis Medical Research Foundation, Minneapolis, MN, USA*
[d] *Butler Hospital and the Department of Psychiatry and Human Behavior, Brown Medical School, Providence, RI, USA*
[e] *Department of Psychiatry, Impulse Control Disorder Clinic, University of Minnesota, Minneapolis, MN, USA*

Introduction

Obsessive compulsive disorder (OCD) is one of the most disabling mental illnesses globally. Over the past 30 years, clinical trials have resulted in several successful pharmacotherapies for OCD yet patients in clinical settings often report little or no response. This study compares the socio-demographic and clinical characteristics of a large sample of community members with OCD to the inclusion/exclusion criteria used throughout pharmacotherapy trials.

Methods: The sample was obtained from the Brown Longitudinal Obsessive Compulsive Study consisting of 325 community members with a DSM-IV diagnosis of OCD. MedLine, PubMed, and professional library resources were searched for studies published between 1980–2010 using the keywords obsessive compulsive disorder, efficacy, pharmacotherapy, medication, double-blind, placebo-controlled, clomipramine, fluoxetine, paroxetine, sertraline, and fluvoxamine. We estimated the proportion of patients in each decade satisfying the most common inclusion/exclusion criteria (operationalized as criteria present in ≥65% of the clinical trials). Pearson correlation estimates were calculated among criteria.

Results: Forty-two clinical trials were included in the analysis. Overall, 72.0% [95% CI: 66.8% - 76.8%] of the 325 subjects included in this sample would have been excluded from trials conducted between 1980–2010. The exclusion rate was dramatically lower between 1980–1989 when only 19.7% the sample would have been excluded but rose to 74.8% for trials conducted between 1990–1999 and 76.9% between 2000–2010.

Conclusions: Over the past 20 years, the majority of community members with OCD would not qualify for OCD treatment studies due to high depression scores, co-occurring anxiety disorders, and a failure to meet threshold criteria for clinical severity based upon measures like the Yale Brown Obsessive Compulsive Disorder rating scale. Given the low rates of treatment response and recent trend in pharmacotherapeutic augmentation studies for OCD, this study illustrates the need to include a more community-representative sample of patients with OCD in clinical trials examining pharmacotherapy efficacy.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Shifting and stopping of prospective memory (PM) responses in obsessive-compulsive disorder (OCD)

Demeter G.Y.[a], Csigó K.[b], Harsányi A.[b], Németh A.[b], Racsmány M.[a]

[a] *BME, Department of Cognitive Science, Egry József 1, Budapest, Hungary, 1111.*
[b] *Department of Psychiatry, Gyula Nyírő Hospital, Budapest, Hungary*

Keywords: Executive functions; Shifting; Inhibition; Prospective memory; Obsessive-compulsive disorder

Introdution

Here we present two experiments aimed to investigate prospective and inhibitory memory functions in OCD. In the first experiment we adapted an experimental paradigm developed by Burgess et al. (2001), who demonstrated that different cortical areas are implicated in the maintenance and in the realization of an intention. According to our results the OCD group performed significantly slower on this task than a matched healthy control group. A further aim of our study was to find different performance patterns related to two subgroups of OCD patients subdivided by their scores on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). The so-called *compulsive subgroup* performed significantly slower on the expectation condition relative to the baseline condition, while the *obsessive subgroup* produced impaired performance on the execution of the prospective task.

In the second experiment we applied a modified dual-task paradigm which required the altered execution and inhibition of responses to the same secondary task cues. We found that OCD patients made significantly more false alarm type errors and there was a significant positive correlation between the number of false alarms and the PM subscale scores of the Prospective Retrospective Memory Questionnaire (PRMQ). These results suggest that OCD patients experience difficulties during event-based PM task and that these difficulties may originate from over-monitoring stimuli for possible PM cues and the disinhibition of activated out-of-date responses.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Obsessions, as problems of thought suppression; compulsions, as behavioral-executive impairment

András Harsányi (*)[a], Katalin Csigó [a], Csaba Rajkai [a], Gyula Demeter [b], Attila Németh [c], Mihály Racsmány [b]

[a] *Nyírő Gyula Hospital, II Psychiatric Department, Lehel út 59, 1135. Budapest, Hungary.*
[b] *BME, Department of Cognitive Science, Egry József 1, Budapest, Hungary, 1111.*
[c] *Semmelweis University, Department of Psychiatry, Balassa utca 6. 1083. Budapest, Hungary*

Introdution

Impairments in executive functioning have been identified as an underlying cause of obsessive-compulsive disorder (OCD). Obsessive patients attempt to suppress certain unwanted thoughts through a mechanism that Wegner referred to as 'chronic thought suppression', whereas compulsive patients are unable to inhibit their rituals. We tested 51 OCD patients using the Yale-Brown Obsessive Compulsive Scale (*Y-BOCS*), the White Bear Suppression Inventory (WBSI) and the Dysexecutive Questionnaire (DEX). Executive functions were tested using a cognitive test battery. We found that the total WBSI score was correlated with the Y-BOCS obsessive score but not with the Y-BOCS compulsive score. A stronger correlation was observed between the Y-BOCS obsessive score and the 'unwanted intrusive thoughts' factor based on Blumberg's 3-factor model of the WBSI. The total WBSI score was not correlated with the cognitive test results. The DEX score was significantly correlated with the Y-BOCS compulsive score; however, no correlation was found between the DEX score and the Y-BOCS obsessive score. A stronger correlation was observed between the Y-BOCS compulsive score and the 'inhibition' component of the DEX score, as defined by Burgess's 5-factor model. The DEX scores were correlated with cognitive test results measuring attention, cognitive flexibility and inhibitory processes. We conclude that obsessions indicate a failure of cognitive inhibition but do not involve significant impairment of executive functions, whereas compulsions indicate ineffective behavior inhibition and impaired executive functions.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Executive function performance in subjects with PANDAs

Nicolini H.[a,b,c], Flores J.[a], Lanzagorta N.[c], Genis-Mendoza A.D.[a,b], De la Fuente-Sandoval C.[d], Santana D.[c]

[a] *Servicios de Atención Psiquiátrica (SAP), Secretaria de Salud, Mexico City, Mexico.*
[b] *Universidad Autónoma de la Ciudad de México (UACM), Mexico City, Mexico.*
[c] *Grupo Médico Carracci, Mexico City, Mexico.*
[d] *Departamento de Neuropsiquiatría, Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez, Mexico City, Mexico.*

Background

OCD-PANDAS is an immune condition that produces neural alterations predominantly in fronto-subcortical networks, inducing early onset OCD (as well as Tics and Tourette). Early onset OCD has been recognized as a different clinical condition (often more severe) than late onset OCD. Cognitive and neuropsychological characteristics in PANDAS are insufficiently described in literature, particularly for executive functions (oriented to characterize frontal-subcortical disfunction). The goal of this study was to assess the neuropsychological performance of a group of PANDAS.

Methods: We evaluated 22 patients with early onset-OCD whom have been identified (confirmed by immunology tests) as possible PANDAS. Age subject range was10 to 43 years old, all adolescents were attending school, adults ranged from 10 to 18 school-years. An Executive function battery (including WCST-64 modified version, Iowa-type test, Hanoi Tower, verbal and visual working memory, verbal fluency, Stroop effect) has been applied. Neuropsychological performance in patients was compared to a control group paired by age, sex, and school-years.

Results: As a group PANDAS-subjects presented a (statistically significant) deficiently performance: 1) at the Iowa-type test (with problems to avoid high risk choices), 2) lower scores in both working memory modalities verbal and/or visual, 3) Higher number of errors in attention control (non-stroop type errors), and 4) Problems in classifying categories (total number of errors at WCST-64 modified version) and slowness in test performance (cognitive efficiency). Frequency of neuropsychological alterations in total sample were: 61% in risk-detection, 57% in working memory (verbal and or visual), 47% in mental inflexibility, 42% at risk-benefit processing, 36% in verbal fluency and 36 % in visual-spatial planning.

Conclusions: These findings mainly suggest that OCD-PANDAS have deficits in frontal-orbital, as well as prefrontal-dorsolateral regions of the brain.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Olfactory identification deficit and its association to response inhibition in obsessive-compulsive disorder: on the scent of the orbitofronto-striatal model.

G. Bersani [a], A. Gallo [b], A. Quartini [a], F. Ratti [a], F.S. Bersani [a], G. Pagliuca [b]

[a] *DSM ASL/LT-Unity of Psychiatry, Department of Medico-Surgical Sciences and Biotechnologies*
[b] *Unit of Otorhinolaryngology, Faculty of Pharmacy and Medicine - "Sapienza" University of Rome, "A. Fiorini" Hospital-Terracina (ITALY)*

Background

Normal olfactory identification (OI) ability is contingent upon the normal functioning of the orbitofrontal cortex (OFC). Tests of smell identification are a well-recognised means of indirectly assessing the integrity of the OFC. The fronto-striatal circuitry involving the OFC has been implicated in the neuropathology of Obsessive Compulsive Disorder (OCD). However, until today, few studies have assessed the olfactory function in OCD and of those studies published, the results are mixed.

Aims: To investigate the olfactory and cognitive functions in patients with OCD compared to healthy control subjects and to relate olfactory function to neuropsychological performance.

Methods: The Brief Smell Identification Test (B-SIT) and tests from the Cambridge Neuropsychological Automated Battery (CANTAB) were administered to 30 patients with OCD and to 22 healthy matched controls. We controlled for age, gender, smoking status and IQ. In OCD patients we also controlled for symptom severity.

Results: A significant impairment in OI ability as well as widely distributed cognitive deficits in visual memory, executive functions, attention, and response inhibition were found in OCD patients relative to controls. Among all the CANTAB tests, and only for the OCD patients, the degree of behavioural impairment on the response inhibition Stop Signal Task [slower Stop Signal Reaction Time (SSTR)] strongly correlated with B-SIT score.

Conclusions: In line with the fronto-striatal dysfunction model of OCD, we confirmed, in a larger number of subjects, our previous observation of a common pathologic process underlying OI and response inhibition impairments in patients with OCD. A slower SSRT has been associated to impulsive behaviours. This is the first study to report OIDs as a predictor of impulsivity in this clinical population. Further exploration of the potential diagnostic utility of OIDs in the assessment of OCD would be useful. Such measures may help delineate the clinical complexity of OCD and support more targeted investigations and interventions.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Brain imaging correlates of olfactory dysfunction in OCD

Segalàs C., Soriano-Mas C., Alonso P., Cardoner N., Real E., López-Solà C., Subirà M., Menchón J.M.

OCD Clinical and Research Unit, Department of Psychiatry, Bellvitge University Hospital, Barcelona, Spain.

Background

Olfactory dysfunction has been described in several neuropsychiatric disorders and specifically in Obsessive Compulsive Disorder (OCD). Brain regions involved in smell processing in healthy people are overlapped with structures implicated in the neurobiological bases of OCD. No previous study has analyzed neuroanatomical correlates of olfactory dysfunction in OCD. The aim of our study was to examine the association between regional gray matter volume assessed by a Voxel-based Morphometry (VBM) analysis of Magnetic Resonance Images (MRI) and olfactory functions, tested by Sniffin' Stick test (SST).

Methods: Olfactory function was assessed in 19 OCD patients and 19 healthy volunteers using the "Sniffin' Stick test". Images from all the sample were acquired with a 1.5-T MRI scanner and precessed with SPM8.

Results: OCD patients showed significant impairment in all of the smell functions (threshold, discrimination and identification) assessed with SST compared to healthy volunteers. Voxel-based mapping of brain structures in healthy controls revealed significant and positive association between threshold score and increase of gray matter volume of the left anterior cingulated cortex. In OCD patients a positive correlation was found between lower identification capacity and increase of gray matter volume of the posterior olfactory sulcus.

Conclusions: Our findings support the hypothesis that some of the olfactory dysfunctions described in OCD are associated with volumetric changes in brain areas implicated in the disorder.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Compensatory frontal-parietal hyperactivation during working memory in patients with obsessive-compulsive disorder and their unaffected relatives: a potential endophenotype.

de Vries F.E.[a], de Wit S.J.[a], Cath D.C.[c], van der Werf Y.D.[b], van der Borden V.[a], van Rossum T.[a], van Balkom A.J.L.M[a], van der Wee N.J. A.[d], Veltman D.J.[a], van den Heuvel O.A.[a,b]

[a] *Department of Psychiatry, VU University medical Center, Amsterdam*
[b] *Department of Anatomy and Neuroscience, VU University medical Center, Amsterdam*
[c] *Academic Anxiety center, Altrecht, Utrecht*
[d] *Department of Psychiatry and Leiden Institute for Brain and Cognition, Leiden University Medical Center, Leiden*

Context

Subtle cognitive deficits exist in patients with obsessive-compulsive disorder (OCD) as well as in unaffected relatives, supporting the putative involvement of frontal and parietal areas in the disorder. We hypothesized a dysfunctional frontal-parietal working memory circuit in both patients and unaffected relatives, constituting a potential endophenotype for OCD.

Methods: Forty-three medication-free OCD patients, 17 unaffected siblings and 37 healthy controls matched on age, gender and IQ underwent functional magnetic resonance imaging while performing a visuo-spatial working memory (*n*-back) task, with a baseline condition and three load levels of increasing difficulty (*1*-back, *2*-back, *3*-back). We compared task (all loads vs. baseline) and load-related activity patterns between groups using a region-of-interest approach including prefrontal (bilateral dorsolateral prefrontal cortex, pre-supplementary motor area, cingulum) and parietal regions (bilateral precuneus and inferior parietal cortex). Results are reported at $p < 0.05$, Family Wise Error corrected.

Results: At *3*-back a performance deficit was present in OCD patients, compared with controls, but not in siblings. Increased task-related activation in left dorsal prefrontal areas and left precuneus was found in patients and in an extended network in siblings (bilateral dorsal prefrontal, parietal and cingulate cortices), compared to controls. However, from *2*-back to *3*-back OCD patients showed relative deactivation in the task-related network in contrast to controls. OCD patients with high performance showed relatively more hyperactivation than patients with low performance. No correlation between OCD symptom severity and brain activity was found. Performance at *3*-back correlated with activity in right pre-supplementary motor area.

Conclusions: Altered activity patterns of the frontal-parietal circuitry of both OCD patients and unaffected siblings during the n-back task may constitute an endophenotype for OCD. We suggest that increased activation in siblings and the high performing OCD patients is compensatory and preserves performance, whereas other OCD patients fail to adequately compensate, resulting in a performance deficit.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Emotion regulation in obsessive-compulsive disorder: a functional MRI study before and after transcranial magnetic stimulation

de Wit S.J.[a], van der Werf Y.D.[b], Mataix-Cols D.[c], van Balkom A.J.L. M.[a], Veltman D.J.[a], van den Heuvel O.A.[a,b]

[a] *Department of Psychiatry, VU University Medical Center, Amsterdam, the Netherlands*
[b] *Department of Anatomy and Neurosciences, VU University Medical Center, Amsterdam, the Netherlands*
[c] *Institute of Psychiatry, Kings College London, London, United Kingdom*

Background

Increased emotional reactivity in obsessive-compulsive disorder (OCD) may be due to a deficit in emotion regulation, caused by a failure of cognitive control exerted by dorsolateral prefrontal cortex (dlPFC). We hypothesized that 1) during emotion regulation, patients with OCD would show deficient recruitment of the dlPFC and that 2) stimulating high-frequency and inhibiting low-frequency repetitive transcranial magnetic stimulation (rTMS) on the dlPFC would improve cognitive control in patients, and diminish it in healthy controls, respectively.

Methods: Forty-three medication-free OCD patients and 38 matched controls performed an emotion regulation task with general fear and OCD-related stimuli during 3-Tesla functional MRI. Pictures were processed in either an 'attend' (passive viewing) or 'regulate' (apply cognitive reappraisal techniques to diminish negative affect) condition. Subjects rated each picture on a distress scale. Subjects were scanned twice: at baseline, and after real or placebo rTMS. We assessed effects of disease-status and rTMS on distress ratings and on brain activity during emotion regulation.

Results: Patients and controls both showed distress reduction in the regulate vs. attend-condition at baseline. During fear regulation, controls recruited the left dlPFC (BA9/46) and bilateral parietal cortex (BA40/7) significantly more than patients. Emotion regulation in patients was characterized by recruitment of dorsomedial PFC, which was significantly more active during OCD-related regulation in patients versus controls.

Controls in the placebo-condition ($p=.02$) and patients in the stimulating-rTMS condition ($p=.10$) showed reduced fear distress scores at day 2 vs. day 1, while scores of controls in the inhibiting-rTMS condition and patients in the placebo-condition did not change. The change in distress ratings over sessions correlated with changes of activation in brain regions involved in emotion processing and regulation.

Conclusions: In line with our 'emotion-dysregulation'-hypothesis, patients with OCD showed deficient recruitment of the dlPFC during emotion regulation. rTMS on dlPFC may affect implicit fear regulation.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Higher glutamate in the associative striatum of pandas related obsessive compulsive disorder patients: A ^{1}H-MRS study

Nicolini H[a,b,c], Alvarado-Alanis P[d], Genis-Mendoza AD[a,b], López Y[e], Basualdo A[a], Manrique V[e], Niubo E[e], Hernández L.[f], Lopez-Canovas L.[e], Riverón A.[a], López-Casamichana M.[a], Flores J.[c], Lanzagorta N.[b], Santana D.[b], Bobes M.A.[e], De la Fuente-Sandoval C.[d,g]

[a] *Universidad Autónoma de la Ciudad de México (UACM), Mexico City, Mexico*
[b] *Grupo Médico Carracci, Mexico City, Mexico*
[c] *Servicios de Atención Psiquiátrica (SAP), Secretaria de Salud, Mexico City, Mexico*
[d] *Laboratorio de Psiquiatría Experimental, Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez, Mexico City, Mexico*
[e] *Centro de Neurociencias de Cuba, Havana, Cuba*
[f] *Clínica Del Adolescente, Havana, Cuba*
[g] *Departamento de Neuropsiquiatría, Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez, Mexico City, Mexico*

Introduction

Neuroimaging studies have provided evidence of cortico-striatal circuitry dysfunctions in obsessive–compulsive disorder (OCD). Although previous studies using proton magnetic resonance spectroscopy (^{1}H-MRS) have shown glutamatergic alterations in these patients, to date no study has been performed in Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections (PANDAS) patients that presents OCD symptoms.

Methods: The aim of this study was to compare, using proton magnetic resonance spectroscopy (^{1}H-MRS), glutamate levels in the precommissural dorsal-caudate (or associative striatum) in 17 PANDAS-OCD patients and 17 age-gender matched controls. All subjects underwent a ^{1}H-MRS study using a 3Tesla scanner (PRESS, TE=35ms, TR=2000ms, voxels=8ml). Glutamate levels were estimated with LCmodel software and corrected for cerebrospinal fluid proportion in the voxel.

Results: Patients showed higher levels of glutamate (T=4.51, p=<0.001), and glutamate + glutamine (T=2.52, p=0.017) in the associative-striatum compared to healthy controls.

Conclusions: The results suggest that a high glutamate level is present in a brain region previously implicated in the pathophysiology of OCD.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Proton Magnetic Resonance Spectroscopy of Orbital Frontal White Matter in Medication Naïve Children with OCD

Weber A.M.[a], Soreni N.[a,b], Stanley J.A.[h], Greco A.[b], Szatmari P.[b], Schachar R.[g], Mannasis K.[b], Pires P.[b], Swinson R.P.[b], Noseworthy M.D.[a,c,d,e,f]

[a] *School of Biomedical Engineering, McMaster University, Hamilton, Ontario, Canada*
[b] *Department of Psychiatry and Behavioural Neuroscience, Hamilton, Ontario, Canada*
[c] *Electrical & Computer Engineering, McMaster University, Hamilton, Ontario, Canada*
[d] *Medical Physics & Applied Radiation Sciences, McMaster University, Hamilton, Ontario, Canada*
[e] *Diagnostic Imaging, St. Joseph's Healthcare, Hamilton, Ontario, Canada*
[f] *Department of Radiology, McMaster University, Hamilton, Ontario, Canada*
[g] *Department of Psychiatry, the Hospital for Sick Children, Toronto, Ontario, Canada*
[h] *Department of Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, MI, USA*

Background

Obsessive-compulsive disorder (OCD) is a neuropsychiatric disorder with a typical onset during childhood or adolescence. Proton magnetic resonance spectroscopy (^{1}H-MRS) allows in vivo measurements of several metabolic markers localized in gray and white matter tissues. To date, however, no *in vivo* ^{1}H-MRS studies have been published that compare brain metabolite levels from white matter between patients and controls under the age of 18. Methods: *In vivo* brain metabolite levels in the left and right orbito-frontal white matter (LOFWM, ROFWM, respectively) were measured in medication-naïve children and adolescents with OCD (LOFWM: N=15, mean age 12.9 years, SD=2.4; ROFWM: N=16, Mean age 13.2 years, SD=2.1) and healthy controls (N=21, Mean age 11.2 years, SD=2.7) using *in vivo* ^{1}H-MRS at 3 Tesla. Spectra were acquired using a single voxel PRESS sequence (1.5x2.0x2.0cm^{3}, TE/TR=30/2000ms, 192 averages) and analyzed using LCModel. Metabolite levels were obtained using the unsuppressed internal water signal method, along with tissue fractions obtained from tissue segmentation and appropriate relaxation times.Results: In the ROFWM, children and adolescents with OCD had statistically significant ($p = 0.003$) higher levels of N-acetyl-aspartate and a trend towards significantly higher levels of glutamate ($p = 0.072$), even when controlling for age and sex. In addition, levels of myo-Inositol in the LOFWM were positively and significantly correlated with severity of OCD symptoms. Discussion/Conclusion: This is the first published study of white matter metabolite levels in children and adolescents with OCD. Our findings of case-control differences in brain metabolite levels, lend further support to the cortico-striato-thalamic-cortical hypothesis of OCD.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

The State of Art of Association between COMT gene and Obsessive-Compulsive Disorder

Sampaio A.S., Quarantini L.C., Teles C., Cappi C., Daltro-Oliveira R., Lins R.P., Hounie A.G., Miguel E.C.

Department and Institute of Psychiatry, University of Sao Paulo Medical School, Serviço Médico Universitário, Universidade Federal da Bahia
Departamento de Neurociências e Saúde Mental, Universidade Federal da Bahia, Hospital Universitário (Com-HUPES), Universidade Federal da Bahia
Instituto de Saúde Coletiva, Universidade Federal da Bahia

Background

Catechol-O-methyltransferase (COMT) is responsible for dopamine metabolism and has been thought to play a role in obsessive-compulsive disorder (OCD)-related pathways by influencing dopamine levels. However, the genetic association between COMT polymorphisms and OCD has not consistent across studies.

Methods: Here, a systematic review and meta-analysis was performed. To interpret the number of genetic association studies between COMT and OCD available in the literature, the Venice Interim Guidelines was established for determining the credibility of the related cumulative evidence.

Results: The systematic review found 23 studies and 21 of them were included in the meta-analysis. Results of the present meta-analysis, together with the literature review, added to the accumulated evidence suggesting a weak association between variants in the COMT Val158Met polymorphism and OCD.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Association between MAO-A and Obsessive-Compulsive Disorder related phenotypes

Sampaio A.S.[a,b], Hounie A.G.[a], Petribú K.[c], Cappi C.[a], Morais I.A.[a], Quarantini L.C.[b], Filho H.P.V.[a], da Conceição do Rosário M.[d], Stewart S.E.[e,f], Fargeness J.[f], Matthews C.[g], Arnold P.[h], Richter M.[h], Kennedy J.[h], Hanna G.L.[i], Pauls D.L.[f], Miguel Filho E.C.[a]

[a] *Department and Institute of Psychiatry, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil*
[b] *Universidade Federal da Bahia (UFBA- Federal University of Bahia), Faculdade de Medicina, Salvador, Brazil*
[c] *Universidade de Pernambuco (UPE, University of Pernambuco) Faculdade de Ciências Mèdicas, Recife, Brazil*
[d] *Universidade Federal de Sao Paulo (UNIFESP, Federal University of São Paulo), São Paulo, Brazil*
[e] *University of British Columbia, Vancouver, BC, Canada*
[f] *Psychiatric and Neurodevelopmental Genetics Unit (PNGU), Massachusetts General Hospital, Boston, MA, USA*
[g] *University of California, San Francisco, CA, USA.*
[h] *University of Toronto, Toronto, ON, Canada*
[i] *University of Michigan, Ann Arbor, MI, USA*

Keywords: Obsessive-Compulsive Disorder; Catechol-O-Methyltransferase; Monoamine Oxidase; Genetic Association Study

Objective

The objective of the present study was to examine association between monoamine oxidase A (*MAO-A*) polymorphisms and obsessive-compulsive disorder (OCD) related phenotypes in 83 Brazilian trios.

Methods: The study sample comprised 83 OCD probands and their parents. Six single-nucleotide polymorphisms were genotyped and transmission disequilibrium was analyzed.

Results: *MAO-A* was associated with a broadly-defined OCD phenotype (when 75% of DSM IV criteria for OCD was met) as well as with OCD spectrum disorders (i.e., anxiety disorders, body dimorphic disorder, skin picking and trichotillomania).

Conclusions: The association between MAOA and obsessive-compulsive symptoms as well as OCD spectrum disorders could bolster the notion that altered *MAO-A* function influences different neurotransmitters and pathways, resulting in low specificity for behavioral changes. Further association studies of OCD-related phenotypes, involving larger independent samples, are required.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Post-mortem brain transcriptional alterations of the HTR2A: correlation with developmental stages and genotypes

Grünblatt E[a,b], Marinova Z[a], Monoranu CM[c], Walitza S[a,b]

[a] *Child and Adolescent Psychiatry, University of Zurich, Neumünsterallee 9, 8032 Zürich, Switzerland*
[b] *Neuroscience Center Zurich, University of Zurich and ETH Zurich, Switzerland*
[c] *Department of Neuropathology, Institute of Pathology, University of Würzburg, Würzburg, Germany*

Abstract

Several studies demonstrated that a single nucleotide polymorphism (SNP), –1438G/A (rs6311), found in the transcriptional control region of the gene that encodes the serotonin-receptor 2A (HTR2A) is associated with obsessive-compulsive disorder (OCD) in particular with the early onset form, starting by age 10. A meta-analysis of our results as well as many other published results point to its association with early-onset OCD. Several studies investigated the effects of the HTR2A imprinting on expression, but up to now there are conflicting results. Still several epigenetic studies suggested that the rs6311 SNP affects methylation status of the promoter region and therefore affects the transcription of HTR2A. Here we investigated in post-mortem brain tissue (in several different brain regions) the transcriptions of HTR2A and correlated it to the developmental stage of the brain (41-weeks foetus in uterus to 85 years old age controls), as well as to the genotype of each of the subjects. The knowledge arising from this study will enable to understand the functional effect of this polymorphism on brain development and expression of the excitatory receptor HTR2A in different brain regions.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Association study between BDNF gene variants and OCD Mexican patients

Márquez L[a], Camarena B[b], Hernández S[b], Lóyzaga C[a], Vargas L[a], Vargas I[b], Nicolini H[c]

[a] *Clinic of Obsessive-Compulsive Disorder and Spectrum Disorders, National Institute of Psychiatry Ramón de la Fuente Muñiz, Mexico, DF, Mexic*
[b] *Department of Psychiatric Genetics, National Institute of Psychiatry Ramón de la Fuente Muñiz, Mexico, DF, Mexico*
[c] *Autonomous University of Mexico City, Mexico, DF, Mexico*

Introduction

Association between Brain-Derived Neurotrophic Factor (BDNF) gene and Obsessive Compulsive Disorder (OCD) was reported in a family-based association study. In this study, we investigate the role of BDNF polymorphic variants (rs6265, rs1519480 and rs7124442) in OCD Mexican patients using a case-control and family-based association design.

Material and Methods: Our sample consisted of 190 OCD patients, 283 control subjects and 109 OCD families. OCD patients fulfilled DSMIV-TR diagnostic criteria and were captured from Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz and Grupo Médico Carracci. DNA analysis of rs6265, rs1519480 and rs7124442 was performed using Taq-Man allelic discrimination assays. Single SNP and haplotype analyses were conducted to determine association between BDNF variants and OCD.

Results: Case-control analysis showed a significant association between rs6265 and OCD. We observed a high frequency of Val/Val genotype and Val allele in OCD patients compared with controls ($\chi^2=21.8$, $p=0.0001$; $\chi^2=22.7$, $p=0.0001$, respectively). Also, rs1519480 analysis showed a high frequency of G allele in OCD patients compared with control group ($\chi^2=27.8$, $p=0.0001$). Haplotype analysis showed a high frequency of A-A-T in OCD compared with control group showing a 2.1-fold increased risk of OCD ($p=0.014$). Clinical characteristics did not show significant differences in SNP and haplotype-based analysis. Finally, the family-based association study did not show linkage disequilibrium.

Conclusions: We replicated the association between Val allele of rs6265 BDNF gene polymorphism and OCD. We found significant association of rs1519480 in OCD patients compared with a control group. Finally, we observed a high risk haplotype (A-A-T) in OCD patients and a protective A-G-T haplotype for OCD. Interestingly, the risk to develop OCD could be dependent of being a carrier of A variant of rs1519480, region that has never been analyzed in OCD. Therefore, our findings suggest that BDNF gene could be related to the development of OCD.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Does inflammation play a role in Obsessive Compulsive Disorder?

Silverman M.[a], Cassab R.[b], Muniz R[b], Shavitt R.G.[b], Toledo M.C.[b], Cappi C.[b], Thayer J.[c], de Mathis A.[b], Diniz J.[b], Hoexter M.[b], Alcante C. D.[b], Borcato S.[b], Hounie A.G.[b], Whitfield J.[a], Belyavskaya E.[a], Sternberg E.[a], Miguel E.[a], Marques A.[a,b]

[a] *Section on Neuroendocrine Immunology and Behavior, National Institute of Mental Health, National Institutes of Health, Bethesda, MD, USA*
[b] *Obsessive-Compulsive Spectrum Disorders Program, Department & Institute of Psychiatry, University of São Paulo Medical School*
[c] *Dept. of Psychology, The Ohio State University, Columbus, OH, USA*

Background

An imbalance between pro and anti-inflammatory cytokines has been described in psychiatric disorders, such as depression and schizophrenia. Immune dysregulation has been hypothesized to play a role in at least some cases of OCD. Studies of cytokines in OCD patients have shown contradictory results and some studies have shown that specific obsessive compulsive symptoms are associated with specific cytokines.

Objectives: The aim of this study was to evaluate the association between cytokine profiles and OCD severity in OCD patients before and after intervention as compared to healthy controls.

Methods: Plasma levels of pro-inflammatory (IL-1α, IL-1β, IL-2, IL-6, IL-8, TNFα and IFNγ) and anti-inflammatory (IL-10, IL-4, TGFβ) cytokines were evaluated in 70 OCD patients and 101 healthy controls. Clinical and immunological evaluations were performed at baseline and 12 weeks later after treatment. The second assessment was performed in 43 OCD patients (59.7%) and 87 healthy controls (86.1%).Cytokine levelswere analyzed by glass chip-based-Ab microarrays. Generalized estimating equations were applied to determine associations between cytokines (continuous and binary) and OCD diagnosis and severity, after controlling for psychotropic medication.

Results: Thirty (43%) OCD patients presented with depression (MDD and/or Dysthymia). Cytokine profiles were similar in OCD patients with depression, OCD patients without depression, and healthy controls; and also in OCD patients before and after treatment. There was no significant association between cytokine levels and YBOCS scores, or between cytokines levels and Beck Depression scores. However, $\log_{10}$ TNFα was associated with reduction in YBOCS scores (0.0104; $p=0.047$); the presence of IL-1β was associated with 81% reduction of YBOCS scores (-0.201, $p=0.046$); and the presence of IFNγ (0.2739, $p=0.028$) was associated with 31% increase of YBOCS scores.

Conclusion: OCD patients (with and without depression) did not exhibit different cytokine patterns compared to healthy controls. However, specific cytokines were associated with OCD severity and treatment response.

Financial Support: NARSAD Joan Granlund Investigator Award, FAPESP (Fundaçao de Amparo à Pesquisa do Estado de Sao Paulo, BRAZIL)

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Association study between 5-HTT and antibody titers in a group of patients of children's onset obsessive-compulsive disorder from Mexico City and Cuba

Nicolini H.[a,b,c], Genis-Mendoza A.D.[a,c], López Y.[d], Basualdo A.[a], Manrique V.[d], Niubo E.[d], Hernández L.[f], Lopez-Canovas L.[d], Riverón A.[a], López-Casamichana M.[a], Flores J.[c], Lanzagorta N.[b], De la Fuente-Sandoval C.[e], Santana D.[b], Bobes M.A.[d]

[a] *Universidad Autónoma de la Ciudad de México (UACM), Mexico City, Mexico*
[b] *Grupo Médico Carracci, Mexico City, Mexico*
[c] *Servicios de Atención Psiquiátrica (SAP), Secretaria de Salud, Mexico City, Mexico*
[d] *Centro de Neurociencias de Cuba, Havana, Cuba*
[e] *Departamento de Neuropsiquiatría, Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez, Mexico City, Mexico*
[f] *Clínica Del Adolescente, Havana, Cuba*

Introduction

Streptococcal infection can lead to an autoimmune disease characterized by a spectrum of psychiatric disorders called PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders). It has been suggested the involvement of the serotoninergic system in the pathophysiology of obsessive-compulsive disorder (OCD), supported by the therapeutic efficacy of selective serotonin reuptake inhibitors (SSRI). Similarly, it is known that serotonin is involved in immunological processes as reported in atopic dermatitis, and the influence of serotonin concentration may

modulate 5-HT1A autoreceptors due to psychological stress. Those individuals, carriers of a particular genotype of 5-HTT, could be related to the amount of antibody titers associated with PANDAS.

Objective: This study assessed the association between 5-HTT genotypes and antibody titers (anti-streptococcal (AS), anti-neural from brain lysate glycoproteins (AN), and anti-enolase (AE)) associated with the PANDAS phenotype in patients from Mexico City and Cuba.

Methods: The study has been approved by an independent ethics committee; all enrolled patients provided a written informed consent. OCD-PANDAS was diagnosed in 50 patients from Mexico and Cuba, according to current clinimetric standards. It was determined the presence of 3 antibodies AS, AN, and AE by ELISA. Besides, DNA from peripheral blood was extracted for 5-HTT genotyping.

Results: The sample was divided into three genotypes (LL, SL and SS) and compared to titers of the three antibodies. Statistically significant differences were observed between the titers of AN with SL and SS genotypes ($p = 0.045$) and also between LL and SS genotypes ($p = 0.018$). Individuals with SS genotypes had higher levels of antibodies that LL. In addition individuals with the SS genotype had also a higher number of titles of AE comparing LL vs SL/SS genotypes ($p = 0.0018$). No differences were found for the AS.

Acknowledgments: We thank ICYT-DF for the support given to this project.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Can early improvement be an indicator of treatment response at twelve weeks in obsessive-compulsive disorder? Implications for early-treatment decision-making

Daniel Lucas Conceição Costa (*)[a], Roseli Gedanke Shavitt [a], Raony Cassab [b], Marinês Alves Joaquim [a], Sonia Regina Borcato [a], Carolina Valério [a], Eurípedes Constantino Miguel [a], Juliana Belo Diniz [a]

[a] *Projeto Transtornos do Espectro Obsessivo-Compulsivo (PROTOC, Obsessive-Compulsive Spectrum Disorders Project), Department and Institute of Psychiatry, Universidade de São Paulo (USP), Schoolof Medicine, São Paulo, Brazil*

[b] *Department of Statistics, Institute of Mathematics and Statistics, Universidade de São Paulo, São Paulo, Brazil*

Background

Non-response to serotonin reuptake inhibitors (SRIs) represents a challenge in obsessive-compulsive disorder (OCD) treatment. Usually, at least 12-weeks are necessary to determine that a patient was not responsive to a SRI. However, early predictors of non-response may be useful to determine if additional interventions can be implemented in the short term. We aimed to investigate if early improvement (at 4 weeks) is a predictor of OCD outcome after 12 weeks.

Methods: We performed a secondary analysis of the results of an SRI trial conducted with 145 OCD patients admitted to an outpatient clinic. Inclusion criteria: age between 18-65 years, DSM-IV primary diagnosis of OCD, minimum baseline Y-BOCS score of 16 and absence of previous adequate pharmacological treatment for OCD. Systematic assessments on OCD severity were taken at baseline, weeks 4 and 12. Treatment response at 12 weeks was defined as 35% or greater decrease in baseline Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) score. Stepwise logistic regression was used to test the relationship between early improvement (at 4 weeks) and treatment response (at 12 weeks) taking into account socio-demographic and clinical characteristics. Different thresholds of early improvement were tested and the sensitivity and specificity of each cut-off point were calculated.

Results: Early improvement defined as a 20% reduction from baseline Y-BOCS scores was able to predict 12-weeks response with 78.4% sensitivity and 60.5% specificity. According to the logistic regression model, only early improvement remained associated with treatment response after 12 weeks (Odds Ratio$= 1.14$, $p < 0.0001$). Only 17 out of 97 patients who have not improved at week 4 were responders at week 12 (Pearson Chi-Square$= 20.6$, $p < 0.001$).

Conclusions: Early improvement predicted 12-week outcome of OCD with good sensitivity and specificity. Its role in early decision making should be investigated in future studies.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

rTMS as an add-on therapeutic tool in treatment-refractory obsessive compulsive disorder

Bencini L MD, Ramella Cravaro V MD, Quercioli L MD, Di Rollo A MD, Pallanti S MD PhD.

Background

The aim of this study was to investigate the therapeutic efficacy of repetitive transcranial magnetic stimulation (rTMS) of the supplementary motor area (SMA) in treatment-refractory OCD.

Methods: We recruited 11 refractory-OCD patients (6 males and 5 females, mean age 33.36 ± 11.96), with a Y-BOCS score > 16 (enrollment is still in progress). All of these patients underwent a simultaneous, bilateral and low frequency (1Hz) SMA-rTMS as an add-on treatment. Refractoriness (indicated by the lack of a significant Y-BOCS score reduction, $< 35\%$), was defined as no/insufficient response following at least two trials with SSRI and one with clomipramine. There was no change of drug therapy for any patient during the study. Patients underwent 15 rTMS sessions (1 per day, 5 per week for 3 weeks). We used Magstim Rapid Stimulator generating biphasic pulses (Magstim Company, Ltd., Whitland, U.K.) with a focal 70-mm, 8-shaped coil. OCD, mood and anxiety symptoms, were rated at baseline, at the 2nd and at the 3rd week, according to Y-BOCS, HAM-A and HAM-D. We assessed rTMS-treatment effects with a two-way analysis of variance (ANOVA), considering time as indipendent factor and rating scale scores as dependent variables.

Results: After 2 weeks of stimulation 4/11 patients (36.4%) resulted responders ($> 25\%$ Y-BOCS score reduction) and 1/11 remitter (YBOCS score < 18). At the end of the 3rd week, 7/11 patients (63.6%) and 3/11 (27.3%) were respectively responders and remitters.

Conclusion: Bilateral, simultaneous and low frequency SMA-rTMS showed to produce a significant improvement in refractory OCD patients, after 3 weeks of stimulation. Further research is needed to establish any differences using a longer period of stimulation, a major sample of patients and a sham-stimulated control group.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

A Case Series of N-acetylcysteine augmentation in treatment resistant obsessive compulsive disorders

Van Ameringen M.[a], Patterson B.[b], Simpson W.[b,c,d]

[a] *McMaster University, Department of Psychiatry and Behavioural Neurosciences, St. Joseph's Healthcare Hamilton, 301 James St. S. Hamilton ON, Canada, L8P 3B6*
[b] *McMaster University, Department of Psychiatry and Behavioural Neurosciences, Macanxiety Research Centre, 1057 Main St. W., L02, Hamilton, ON, Canada, L8S 1B7*
[c] *MiNDS Neuroscience Graduate Program, McMaster University, 1280 Main St. W. Hamilton ON, Canada, L8S 4K1*
[d] *Women's Health Concerns Clinic, St. Joseph's Healthcare Hamilton, 301 James St. S. Hamilton, ON, Canada, L8P 3B6*

Background

Over the past several decades, our understanding of the biological underpinnings of Obsessive Compulsive Disorder (OCD) has significantly increased. There is a general consensus that OCD is associated with abnormalities in the cortico-striato-thalamo-cortical circuitry. Pharmacological treatment investigations have focused on the role of the neurotransmitters serotonin and dopamine. Evidence-based, first-line treatments for OCD include the serotonin reuptake inhibitors (SRI), however, 40-60% of OCD patients do not respond. A wide variety of agents have been examined as adjuncts to standard SRI treatment in cases of treatment resistance, however, no gold-standard approach has been identified. Glutamate dysfunction is now thought to have a role in OCD, and use of glutamatergic treatment agents may hold promise. N-acetylcysteine (NAC) is an amino acid derivative of cysteine, avaliable as a health supplement. It has shown efficacy in OCD-spectrum disorders and in 1 case report of treatment resistant OCD. METHOD: A retrospective chart review of 6 treatment resistant OCD patients who had been treated with NAC for 6-12 weeks. Symptom severity was evaluated at regular clinic visits. RESULTS: Five of 6 patients took NAC for 12 weeks. The mean endpoint dose was 2833.3 $\pm$ 408.2 mg/day. Only one of the six patients responded to treatment with NAC; two patients reported a worsening of symptoms; no patients reported adverse events. CONCLUSIONS: NAC was not effective in this sample of treatment -refractory OCD patients. Whether this result was a function of the mechanism of action of NAC or of the pathophysiology of treatment refractory OCD, remains unclear.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

The Prevalance of Metabolic Syndrome in Patients with OCD

Karamustafalıoğlu O., Yavuz B.G, Özçelik B., Bakım B., Cengiz Y.C., Yumrukçal H., Türkyılmaz E.

Şişli Etfal Teaching and Research Hospital Istanbul Turkey

Objective

This study aimed to examine the prevalence of metabolic syndrome (MetS) in patients with obsessive-compulsive disorder (OCD).

Method: This cross-sectional analysis was performed on 58 outpatients with OCD treated in Şişli Etfal Teaching and Research Hospital Psychiatry Department Istanbul Turkey between June 2009 and December 2009. Study population comprised 44 female (75.9%) and 14 male (24.1%) subjects with a mean age of 36.16 $\pm$ 11.61 years. Psychiatric diagnoses were evaluated using Structured Clinical Interview for DSM- IV (SCID-I). Subjects having three or more of the NCEP Adult Treatment Protocol III criteria were defined as having MetS.

Results: Of the overall population, 11 (19%) had MetS. There was no significant difference between the genders in terms of meeting the criteria for MetS (for females 7/44, 15.9% and for males 4/14, 28.6%; $p=0.29$). The patients with MetS was significantly older than the patients without MetS (46.82 $\pm$ 8.41 years vs. 33.66 $\pm$ 10.86 years, $p<0.001$). The components of MetS did not differ significantly between patients using and not using antipsychotics except HDL cholesterol which was significantly lower in patients treated with antipsychotics (48.74 $\pm$ 10.88 mg/dL vs. 56.90 $\pm$ 13.34 mg/dL, $p=0.02$).

Conclusion: Despite the antipsychotic augmentation, the prevalence of MetS (19%) was relatively low among patients with OCD.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002

Investigation of Gender differences in Body Dysmorphic Disorder

Himanshu Tyagi, MRCPsych, Anusha Govender, MSc, Lynne M Drummond, MRCP MRCPsych

OCD & BDD Service, Springfield University Hospital, 61 Glenburnie Road, London SW17 7DJ United Kingdom

Background

Gender plays an integral part in the perception of one's own body image. However, existing treatments for body image disorders do not use sophisticated gender specific approaches to treatment. A relative lack of research in the gender specific factors appears to be one of the main contributory factors for this discrepancy. This study investigated similarities and differences in patients with Body Dysmorphic Disorder (BDD).

Method: We investigated 54 patients with a diagnosis of BDD, who were assessed between 2008 and 2011 at a specialist centre for OCD and BDD, based in southwest London, UK. Routinely collected standard measures at the time of assessment i.e. Yale Brown Obsessive Compulsive Scale (YBOCS-BDD), Body Dissatisfaction Checklist, Beck Depression Inventory (BDI), Montgomery-Asberg Depression Rating Scale (MADRS), Sheehan Disability Scale (SDS) and sociodemographic information (relationship and employment status) were collated and analysed with respect to gender. Self-report questionnaires i.e. Body Dissatisfaction Checklist, BDI and SDS were completed by the patients prior to the assessment interview. Assessment interviews were conducted by clinicians with specific expertise in the treatment of BDD. Data on the preoccupation with body parts was primarily collected from body dissatisfaction checklist and was supplemented with information reported elsewhere in the assessment and treatment reports.

Results: There were more similarities than differences between the two genders.

Our data suggested that females were more likely to present late for treatment and also not be in a stable relationship at the time of presentation. Males were noted to be less likely to be employed. Males scored slightly higher on all clinician rated instruments i.e. YBOCS- BDD, BDI, MADRS and SDS. However none of these demographic or clinical factors were found to have a statistically significant difference between the two genders.

Males and females did not significantly differ in terms of most of the variables on body dissatisfaction checklist. Statistically significant differences were found only in preoccupation with breasts, hips, skin (face and body) and hair (facial hair and corporal hair, except scalp hair). Our results are similar to previously reported findings in the literature (1).

References: 1. Phillips KA, Diaz SF. Gender differences in Body Dysmorphic Disorder. J Nerv Ment Dis. 1997 Sep;185(9):570-7.

http://dx.doi.org/10.1016/j.jocrd.2013.04.002